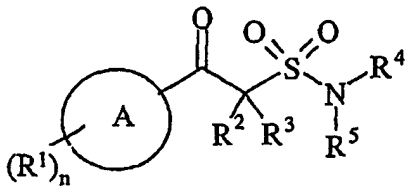
Claims

1. The use of a compound of formula (I):



(I)

wherein:

Ring A is selected from carbocyclyl or heterocyclyl;

R^1 is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino, tri-(C_{1-4}alkyl)silyloxy, carbocyclyl, heterocyclyl, carbocyclylC_{0-4}alkylene-Y- and heterocyclylC_{0-4}alkylene-Y-; wherein R^1 may be optionally substituted on carbon by one or more groups selected from R^6; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^7;

n is 0-5; wherein the values of R^1 may be the same or different;

R^2 and R^3 are independently selected from hydrogen, hydroxy, amino, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, carbocyclyl, heterocyclyl, carbocyclylC_{1-4}alkyl, heterocyclylC_{1-4}alkyl; or R^2 and R^3 together form C_{2-6}alkylene; wherein R^2 and R^3 may be independently optionally substituted on carbon by one or more groups selected from R^8; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^9;

one of R^4 and R^5 is selected from C_{1-4}alkyl and the other is selected from hydrogen or C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon by one or more groups selected from R^{10};

Y is -S(O)$_a$-, -O-, -NR^{12}-, -C(O), -C(O)NR^{13}-, -NR^{14}C(O)- or -SO$_2$NR^{15}-; wherein a is 0 to 2;

R^{12}, R^{13}, R^{14} and R^{15} are independently selected from hydrogen, phenyl and C_{1-4}alkyl;

R^6 and R^8 are independently selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl,

C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino, carbocyclyl and heterocyclyl; wherein R^6 and R^8 may be independently optionally substituted on carbon by one or more R^{11};

R^{10} is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino; wherein R^{10} may be independently optionally substituted on carbon by one or more R^{16};

R^7 and R^9 are independently selected from C_{1-4}alkyl, C_{1-4}alkanoyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonyl, carbamoyl, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl;

R^{11} and R^{16} are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulphinyl, ethylsulphinyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulphamoyl, *N*-ethylsulphamoyl, *N,N*-dimethylsulphamoyl, *N,N*-diethylsulphamoyl or *N*-methyl-*N*-ethylsulphamoyl;

or a pharmaceutically acceptable salt thereof;

in the manufacture of a medicament for use in the inhibition of 11βHSD1.

2. The use according to claim 1 wherein Ring A is pyridyl, phenyl, thienyl, furyl, pyrazinyl, 1,2,3-thiadiazolyl, thiazolyl, cyclohexyl, naphthyl, cyclohexenyl, pyrazolyl, benzothienyl, indolyl, 1,1,3-trioxo-2,3-dihydro-1,2-benzisothiazolyl, 1,3-benzodioxolyl, cyclopentyl, tetrahydropyranyl, 1-oxooctahydropyrido[1,2-a]pyrazinyl, 1,2,3,4-tetrahydronaphthyl, piperidinyl and benzthiazolyl.

3. The use according to either of claims 1 or 2 wherein R^1 is selected from halo, nitro, cyano, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, tri-(C_{1-4}alkyl)silyloxy, carbocyclyl and heterocyclylC_{0-4}alkylene-Y-; wherein R^1 may be optionally substituted on carbon by one or more groups selected from R^6; wherein

Y is $-NR^{12}-$;

R^{12} is hydrogen; and

R^6 is selected from halo, C_{2-4}alkenyl, C_{1-4}alkanoyl, C_{1-4}alkanoylamino and carbocyclyl.

4. The use according to any one of claims 1-4 wherein n is 0-2; wherein the values of R^1 may be the same or different.

5. The use according to any one of claims 1-5 wherein R^2 and R^3 are independently selected from hydrogen or C_{1-4}alkyl, or R^2 and R^3 together form C_{2-6}alkylene.

6. The use according to any one of claims 1-6 wherein one of R^4 and R^5 is selected from hydrogen and C_{1-4}alkyl and the other is selected from C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon by one or more groups selected from R^{10}; and

R^{10} is selected from C_{1-4}alkoxy and *N,N*-(C_{1-4}alkyl)$_2$amino.

7. The of a compound of formula (I) (as depicted in claim 1) wherein:

Ring A is carbocyclyl or heterocyclyl;

R^1 is selected from halo, nitro, cyano, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, tri-(C_{1-4}alkyl)silyloxy, carbocyclyl and heterocyclylC_{0-4}alkylene-Y-; wherein R^1 may be optionally substituted on carbon by one or more groups selected from R^6; wherein:

Y is $-NR^{12}-$;

R^{12} is hydrogen; and

R^6 is selected from halo, C_{2-4}alkenyl, C_{1-4}alkanoyl, C_{1-4}alkanoylamino and carbocyclyl;

n is 0-3; wherein the values of R^1 may be the same or different;

R^2 and R^3 are independently selected from hydrogen or C_{1-4}alkyl, or R^2 and R^3 together form C_{2-6}alkylene;

one of R^4 and R^5 is selected from hydrogen and C_{1-4}alkyl and the other is selected from C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon by one or more groups selected from R^{10}; and

R^{10} is selected from C_{1-4}alkoxy and *N,N*-(C_{1-4}alkyl)$_2$amino;

or a pharmaceutically acceptable salt thereof;

in the manufacture of a medicament for use in the inhibition of 11βHSD1.

8. A compound of formula (I) as depicted in claim 1 selected from:

(4-fluorophenyl)[*N*-(2-methoxyethyl)-*N*-(methyl)sulphamoylmethyl]ketone;

(2,4-difluorophenyl)[1-(*N,N*-diisopropylsulphamoyl)-1methylethyl]ketone;

(2,4-difluorophenyl)(*N,N*-diisopropylsulphamoylmethyl)ketone;

(thiazol-2-yl)(*N,N*-dimethysulphamoylmethyl)ketone;

(4-fluorophenyl)[*N*-(2-isopropoxyethyl)-*N*-(isopropyl)sulphamoylmethyl]ketone;

(pyrazin-2-yl)(*N,N*-dimethysulphamoylmethyl)ketone;

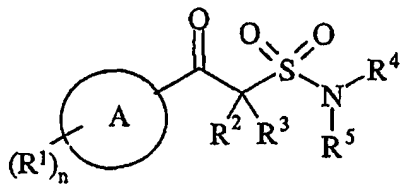
(4-isopropoxyphenyl)(*N,N*-diisopropylsulphamoylmethyl)ketone;

(3-cyanophenyl)(*N,N*-diisopropylsulphamoylmethyl)ketone;

(pyrid-2-yl)(*N,N*-dimethysulphamoylmethyl)ketone;

or a pharmaceutically acceptable salt thereof.

9. A compound of formula (Ia):



(Ia)

wherein:

Ring A is selected from phenyl, pyridyl, thiazolyl, thienyl and furyl;

R^1 is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino; wherein R^1 may be optionally substituted on carbon by one or more groups selected from R^6; and wherein

if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^7;

n is 0-3; wherein the values of R^1 may be the same or different;

R^2 and R^3 are independently selected from hydrogen, hydroxy, amino, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, carbocyclyl, heterocyclyl, carbocyclylC_{1-4}alkyl, heterocyclylC_{1-4}alkyl; wherein R^2 and R^3 may be independently optionally substituted on carbon by one or more groups selected from R^8; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^9;

R^4 and R^5 are independently selected from C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon by one or more groups selected from R^{10};

R^6 and R^8 are independently selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino; wherein R^6 and R^8 may be independently optionally substituted on carbon by one or more R^{11};

R^{10} is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino; wherein R^{10} may be independently optionally substituted on carbon by one or more R^{16};

R^7 and R^9 are independently selected from C_{1-4}alkyl, C_{1-4}alkanoyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonyl, carbamoyl, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl;

R^{11} and R^{16} are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio,

ethylthio, methylsulphinyl, ethylsulphinyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulphamoyl, *N*-ethylsulphamoyl, *N,N*-dimethylsulphamoyl, *N,N*-diethylsulphamoyl or *N*-methyl-*N*-ethylsulphamoyl;

or a pharmaceutically acceptable salt thereof; with the proviso that said compound is not (*N*-methyl-*N*-butylsulphamoylmethyl)(phenyl)ketone; [1-(*N,N*-dimethylsulphamoyl)ethyl](phenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(4-nitrophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(4-fluoro-2-methylaminophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(3-methoxy-4-methyl-6-aminophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(3-methoxy-6-aminophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(phenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(2-nitro-4-methoxyphenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(2-amino-4-methoxyphenyl)ketone; [1-(*N*-methyl-*N*-butylsulphamoyl)ethyl](phenyl)ketone; or (*N,N*-dimethylsulphamoylmethyl)(thien-2-yl)ketone.

10. A pharmaceutical composition which comprises a compound of formula **(I)** or **(Ia)**, or a pharmaceutically acceptable salt thereof, as claimed in either of claims 8 or 9 in association with a pharmaceutically-acceptable diluent or carrier.

11. A compound of the formula **(I)** or **(Ia)**, or a pharmaceutically acceptable salt thereof, as claimed in either of claims 8 or 9, for use in a method of prophylactic or therapeutic treatment of a warm-blooded animal, such as man.

12. A compound of the formula **(I)** or **(Ia)**, or a pharmaceutically acceptable salt thereof, as claimed in either of claims 8 or 9, for use as a medicament.

13. The use of a compound of the formula **(I)** or **(Ia)**, or a pharmaceutically acceptable salt thereof, as claimed in either of claims 8 or 9, in the manufacture of a medicament for use in the production of an 11βHSD1 inhibitory effect in a warm-blooded animal, such as man.

14. The use of a compound as claimed in any one of claims 1-7 or 13 wherein production of, or producing an, 11βHSD1 inhibitory effect refers to the treatment of metabolic syndrome.

15. The use of a compound as claimed in any one of claims 1-7 or 13 wherein production of, or producing an, 11βHSD1 inhibitory effect refers to the treatment of diabetes, obesity, hyperlipidaemia, hyperglycaemia, hyperinsulinemia or hypertension, particularly diabetes and obesity.

16. The use of a compound as claimed in any one of claims 1-7 or 13 wherein production of, or producing an, 11βHSD1 inhibitory effect refers to the treatment of glaucoma, osteoporosis, tuberculosis, dementia, cognitive disorders or depression.

17. A method for producing an 11βHSD1 inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (I), as claimed in any one of claims 1-8, or a compound of formula (Ia) as claimed in claim 9, or a pharmaceutically acceptable salt thereof.